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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/537,180	03/29/2000	Donald R. Owen	WPB40219A	6869

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EXAMINER

SAUCIER, SANDRA E

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/537,180

Applicant(s)

OWEN ET AL.

Examiner

Sandra Saucier

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 224,228,229 and 232-292 is/are pending in the application.
- 4a) Of the above claim(s) 268-292 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 224,228,229 and 232-267 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 March 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 224, 228, 229, 232-292 are pending. Claims 224, 228, 229, 232-267 are considered on the merits. Claims 268-292 are withdrawn from consideration as being drawn to a non-elected invention.

Please cancel the non-elected claims as instructed in the final office action of 12/17/03 in order to prepare the application in the event of allowance.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections – 35 USC § 112

NEW MATTER

Claims 229 and 233 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 229 recites “about 20°C to about 24°C”. Please show literal support for the use of “about” with this range.

Claim 233 recites “about 4°C to about 10°C. Please show literal support for the use of “about” with this range.

Applicant is not free to introduce new elements and broaden ranges after the filing date of the application.

Claim Rejections – 35 USC § 103

Claims 224, 228, 229, 232-245, 248-252, 255, 258-266 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05261 [N].

The claims are directed to a method of maintaining and restoring the viability of an organ subjected to ischemia comprising:

perfusing the organ with a first fluid at a first temperature to maintain/restore pre-ischemia energy levels in the organ, and

perfusing the organ with a second fluid containing substantially no oxygen at a second temperature to store/transport the organ, whereby the second temperature is lower than the first temperature, wherein the first temperature is from about 12°C to about 24°C.

The references are relied upon as explained below.

WO 88/05261 discloses in Example 3, a first normothermic (37°C) perfusion of a FC-43 emulsion at a pressure of 40–120mm Hg followed by a second perfusion with a hypothermic (4–6°C) electrolyte solution at a pressure of <20mm Hg. The perfusate is circulated through a pH sensor module (page 25, l. 20) which is a viability marker or indicative of the organ's viability according to the specification at page 15, l. 28. The perfusate is recycled through a recirculation loop which contains a filter (Fig 1, 16). The recycled perfusate is debubbled and oxygenated and pH regulated prior to returning to the organ. The perfusion may be continuous during storage. The organ is first removed from the subject and cooled in a saline/icewater bath (page 22, l. 10) and perfused with a cardioplegia solution prior to perfusing with the first and second solutions. The organ is stored after the second perfusion in a chamber with includes a housing and an organ supporting surface which allows effluent to pass through, the housing includes openings.

The FC-43 emulsion is an oxygen carrying solution which contains dextrose, both of which function to maintain energy levels in organs (See Ingwall *et al.* [U]). The solution contains oxygen and the partial pressure of oxygen is monitored during the perfusion process. Thus the solution is

considered to have a viability marker as disclosed on page 6, l. 19 of the specification.

The electrolyte solution contains mannitol which is an antioxidant (See Burdon *et al.* [V]).

Insofar as the process relies on the use of components of the solutions which instead of being characterized by technical features suitable for the identification of a solution composition, is imprecisely defined by means of functional features which merely recite the desired result to be achieved, the subject matter is considered to be anticipated or made obvious by the disclosures of the prior art.

Portable is a term without a reference point. Everything is portable if a large enough moving force is applied. Thus, the chamber (1) of the prior art which holds the artificial pericardial sack (2) and has inlets (51) and outlets (16) connected to the organ, can be portaged and thus the chamber is considered to be portable. That the applicants have termed the pericardial sack (2) a "cassette" is the prerogative of the inventor and as it is lacking in structural elements is of little patentable weight. Please note the artificial pericardial sack may be thrown away after use if wished, thus it may be termed "disposable". The container is capable of maintaining the organ at a temperature of 10°C at least for a short period of time because the heart has been cooled. No length of time of the "maintaining" limitation is seen. Maintaining can be for one minute, one hour, or less.

The reference specifically lacks the temperature limitation for the first solution perfusion which is now about 12–24°C. Instead the first perfusion is performed at 37°C.

With regard to the limitation of the first temperature being about 12°C to about 24°C, WO 88/05261 teaches the first temperature of 37±1°C. The instant specification teaches a range of 10–38°C for the first solution. Thus, the new

range limitation is merely an optimization of ranges and is still considered to be obvious over the prior art in the absence of criticality. See MPEP 2144.05 II.A. Also, please note on page 21, lines 15–20, that at temperatures below 20°C, the mitochondria are unable to produce energy. Use of temperatures below 20°C, therefore would not be expected to contribute to restoring energy levels in the organ. Evidence to the contrary might provide unexpected results.

Claim 255 is directed to transplanting the organ into the recipient while the organ remains at the second temperature which is the at temperature that it last was perfused.

While WO 88/05261 does not teach any specific temperature that the heart must be during transplantation, in the absence of evidence to the contrary, one of skill in the art may chose to transplant a cold organ or a warm one as desired.

Claims 246 and 247 remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05261 [N] in view of WO 96/29864 [O]

The claims are further directed to the use of a pressure source incapable of providing pressures greater than 100 mmHg or 40 mmHg.

WO 88/05261 discloses using 40–120 mm Hg pressures in normothermic perfusion and less than 20 mm Hg pressures in hypothermic perfusion. The system is equipped with a pressure release control system which is programmable so as not to exceed a preestablished limit (page 14, ls. 1–10). Fig 4 shows the control systems. The reference lacks the disclosure of using a setting of 100 mmHg which cannot be exceeded.

WO 96/29864 discloses an apparatus used for normothermic perfusing of organs with a pressure maximum of 90 mmHg (page 23).

One of skill in the art may set the pressure in the apparatus of WO 88/05261 so that the fluid perfusion pressure can not exceed 90 mmHg as taught by WO 96/29864 because the apparatus of WO 88/05261 has variable settings which once established according to the desire of the operator will not be exceeded. One of skill in the art would be expected to be able to establish maximal settings of 90 mmHg using the apparatus of WO 88/05261 and the maximal pressure settings as disclosed in WO 96/29864 in the absence of evidence to the contrary.

Clearly the apparatus is capable of operating at pressures no greater than 20mmHg also because this is the setting taught for hypothermic perfusion.

Claims 253 and 254 remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05261 [N] in view of Chambers *et al.* [W].

The claims are directed to the use of antioxidants in the flush solution.

WO 88/05261 is relied upon as discussed above and lacks the specific teaching of the use of antioxidants in the flush/cardioplegic solution.

Chambers *et al.* disclose that the addition of various antioxidants to cardioplegic solutions improves organ viability.

The addition of an antioxidant to the flush, cardioplegic solution of WO 88/05261 (p. 22, l. 6) would have been obvious when taken with Chambers *et al.* who teach the improved viability of a heart when the flush/cardioplegic solution incorporates antioxidants.

Claim 257 remains rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05261 [N] and Ingwall *et al.* [U] or WO 97/43899 [P].

The claim is directed to perfusing the organ with the first fluid at the first temperature prior to transplantation.

WO 88/05261 teaches at page 23, that it is possible to raise the temperature of the heart if there is ATP depletion prior to transplantation.

WO 97/43899 disclose that warming a heart (page 10, l. 23) and perfusing with a solution containing substrates such as glucose (page 10, l. 33) and oxygen (page 11, l. 3) reestablishes oxidative metabolism, which means that ATP levels are established (abstract and Fig. 1).

Inwall *et al.* teaches that ATP levels can be restored in heart when perfusion with a solution containing oxygen and glucose (abstract).

One of skill in the art, given the teaching that one should raise the temperature of the heart if there is ATP depletion (WO 88/05261), would perfuse with the first fluid at the first temperature because warm perfusion of the heart with oxygen and glucose is known to raise endogenous ATP levels and improve viability of the organ as taught by Ingwall *et al.* or WO 97/43899 [M].

Claims 259–266 remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05261 [N] in view of US 5,586,438 [A].

The claims are directed to a method of perfusing an organ in a portable perfusion unit capable of maintaining the organ at a temperature of 10°C or less. Other claims are directed to storing the organ after perfusion with the first medical fluid at the first temperature or with the second medical fluid at the second temperature.

The references are relied upon as explained below.

WO 88/05261 has been discussed above and lacks specific mention of portability.

US 5,586,438 discloses an apparatus for transporting and preserving organs (Fig. 3). It comprises a housing and an organ container. The apparatus can be cooled by ice or other thermal buffers or by the expansion of compressed gas. The preferred temperature of storage/transportation is 6°C (col. 9, l. 29). While the organ container is not disclosed as being disposable, anything in the absence of structural elements can be disposed of. The organ container is removable from the housing and thus, can be thrown away separate from the housing.

The use of the perfusion regimen of WO 88/05261 in the apparatus of US 5,586,438 would have been obvious because one of skill in the art may choose any perfusion apparatus in the art that will perform a specific perfusion regimen. The apparatus of US 5,586,438 is capable of performing the perfusion regimen taught in WO 88/05261 and is used for perfusion and transportation of organs for transplantation.

Further, it is well within the purview of one of skill in the art to store/transport the organ after the perfusion of any solution known in the art at any temperature used in the art in the absence of any evidence of criticality.

Claim 267 remains rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05261 [N] and US 5,586,438 [A] as applied to the claims above, and further in view of US 5,450,329 [B].

The claims are further directed to the use of a GPS to monitor the location of the organ.

WO 88/05261 and US 5,586,438 are relied upon as discussed above. The references lack mention of the use of GPS to track the organ.

US 5,450,329 discloses the use of GPS to track a vehicle.

The use of GPS to track a vehicle which is carrying the portable perfusion unit of US 5,450,329 which contains an organ perfused with the regimen of WO 88/05261 and is intended for transplantation is well within the purview of one of skill in the art because such tracking devices are known in the art.

One of ordinary skill in the art would have been motivated at the time of invention to make these substitution in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

No critical or novel element is seen in the claims. It appears that all elements are known in the art of transplantation.

APPLICANTS' ARGUMENTS

Applicants' arguments filed 9/22/03 have been fully considered but they are not persuasive.

Applicants argue that the cited reference does not disclose maintaining and/or restoring pre-ischemia or pre-hypoxia energy levels in the organ where the first perfusion temperature is 12–24°C.

The insertion of the new limitation has overcome the anticipation rejection over WO 88/05261.

However, the newly limited range is still considered to be obvious in the absence of evidence of criticality. Attention is also drawn to applicant's specification on page 21, where it is stated that the mitochondria are unable to utilize oxygen to produce energy at temperatures below 20°C. Thus, the demonstration of use of temperatures below 20C to maintain and restore energy levels in an organ might be persuasive of unexpected results. Please note that applicants range in which energy levels are restored and maintained

are from 12–24°C in the independent claim and even lower in some dependent claims.

Applicants have not demonstrated that the prior art method which appears to have the similar active steps as the instant method AS CLAIMED does not yield the same result as the instant method. A method having similar active steps would reasonably be expected to give the same result.

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not applicants' result differs and, if so, to what extent from the result discussed in the reference.

Accordingly, it has been established that the prior art method, which has the same active steps and shares the property of being able to preserve organs for transplantation demonstrates a reasonable probability that it is either identical or sufficiently similar that whatever differences exist are not patentably significant. Therefore, the burden of establishing novelty or unobviousness by objective evidence is shifted to applicants. Applicants have not met this burden on the record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272–0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272–0926. The fax phone number for the organization where this application or proceeding is assigned is 703–872–9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sandra Saucier
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Art Unit 1651